
Sequence Listing could not be accepted due to errors.

See attached Validation Report.

If you need help call the Patent Electronic Business Center at (866)

217-9197 (toll free).

Reviewer: Anne Corrigan

Timestamp: [year=2011; month=4; day=22; hr=9; min=53; sec=48; ms=413;]

Reviewer Comments:

<120> Method for detecting LDL receptor gene mutations associated with

Please complete the above "<120>" response: "Method for detecting LDL receptor gene mutations associated with Familial Hypercholesterolemia"

(Sequence 1 has many errors. Errors shown below)

<220>

<221> gene

<223> n at position 35360 represents aau, aac or aat

<220>

<221> gene

<223> n at position 35361 represents aau, aac or aat

Errors above: a single "n" can only represent a single nucleotide, not a codon.

cctctgcctc ctgggttcaa gcgattttcc tgcctcagcc tcccgagtag ctgggattac 8160 aggtgcttgc caccataccc ggctaatttt gtatttttag tagagacggg gttacgccaa 8820

The "8820" above is incorrect: the cumulative nucleotide total should be "8220". Please check all succeeding cumulative nucleotide totals in Sequence 1 for accuracy: mistakes have been noted.

actgcctggc agaggctgcg agc atg ggg ccc tgg ggc tgg aaa ttg cgc 15350 Met Gly Pro Trp Gly Trp Lys Leu Arg

-21 -20 -15

tgg acc gtc gcc ttg ctc ctc gcc gcg gcg ggg act gca g gtaaggcttg 15400

Trp Thr Val Ala Leu Leu Leu Ala Ala Gly Thr Ala -10 -5 -1 1

The above misaligned amino acids are samples of TAB codes appearing throughout Sequence 1: please remove all TAB codes, and align the amino acids and amino acid numbers, properly. Do not show TAB codes in the sequence listing.

Asp Ile Asp Glu Gys Gln Asp

335

Cys Gln Cys Glu Glu Gly Phe Gln Leu Asp Pro His Thr Lys Ala Cys 360 365 370

aag gct gtg g gtgagcacgg gaaggcggcg ggtgggggcg gcctcacccc 36784 Lys Ala Val

375

Besides TAB codes causing misalignment, "Gys" (in the top amino acid row above) is an invalid amino acid designator.

<210> 2

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> Ex1F

Please remove the extra blank space between "Artificial" and "Sequence" in the above "<213>" response. Only one blank space should separate "Artificial" and "Sequence". Same error in many subsequent sequences.

As an explanation of "<213> Artificial Sequence", the above "<223>" response needs more information regarding the source of the genetic material. If this is a primer, please add that to the "<223>" response. Same type of response in subsequent sequences.

<211> 20

<212> DNA

<213> artificial sequence

<220>

<223> probe

<400> 90

cactctcggg cccctaccc

20

Although the above "<211>" response is "20", only 19 nucleotides are shown. The second group of nucleotides totals "9".

<210> 232

<211> 25

<212> DNA

<213> artificial sequence

<220>

<223> probe

<400> 232

ttgtccttgc agtcggggcc acta

Although the above "<211>" response totals "25", only 24 nucleotides are shown. The last group totals "4".

Suggestion: please consult the Sequence Rules for valid format.

25

To correct the sequence listing errors noted in this report - The recommended method for correction of errors is to access the sequence listing working file using the software program in which the listing was originally prepared, e.g., the project file in PatentIn, make any necessary corrections within that program, then generate a new sequence listing file. Use of a word processing program to correct errors directly in the original sequence listing file is strongly discouraged, since such programs often introduce unintended changes to the sequence listing, rendering the listing unacceptable. When the working file or original program is not available for correction, then use of a common

or plair	text-onl	y editor,	such as	NotePad,	to	edit	the	original
sequence	listing	file may	suffice.					

Validated By CRFValidator v 1.0.3

Application No: 10542937 Version No: 4.0

Input Set:

Output Set:

Started: 2011-04-13 11:37:43.725

Finished: 2011-04-13 11:38:01.699

Elapsed: 0 hr(s) 0 min(s) 17 sec(s) 974 ms

Total Warnings: 277

Total Errors: 414

No. of SeqIDs Defined: 259

Err	or code	Error Description
E	254	The total number of bases conflicts with running total, Input: 8820, Calculated: 8220 SEQID(1)
W	333	tabs used in amino acid numbering SEQID (1)
W	333	tabs used in amino acid numbering SEQID (1)
E	254	The total number of bases conflicts with running total, Input: 18940, Calculated: 19840 SEQID(1)
E	254	The total number of bases conflicts with running total, Input: 20190, Calculated: 20200 SEQID(1)
E	254	The total number of bases conflicts with running total, Input: 22700, Calculated: 22720 SEQID(1)
W	333	tabs used in amino acid numbering SEQID (1)
W	333	tabs used in amino acid numbering SEQID (1)
W	333	tabs used in amino acid numbering SEQID (1)
E	323	Invalid/missing amino acid numbering SEQID (1) POS (61)
E	254	The total number of bases conflicts with running total, Input: 28210, Calculated: 28260 SEQID(1)
W	333	tabs used in amino acid numbering SEQID (1)
W	333	tabs used in amino acid numbering SEQID (1)
W	333	tabs used in amino acid numbering SEQID (1)
E	254	The total number of bases conflicts with running total, Input: 39861, Calculated: 30861 SEQID(1)
W	333	tabs used in amino acid numbering SEQID (1)
W	333	tabs used in amino acid numbering SEQID (1)

Output Set:

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Total Warnings: 277
Total Errors: 414
No. of SeqIDs Defined: 259

Error code		Error Description
E	323	Invalid/missing amino acid numbering SEQID (1)at Protein (135)
E	323	Invalid/missing amino acid numbering SEQID (1) POS (136)
E	323	Invalid/missing amino acid numbering SEQID (1) at Protein (140)
E	323	Invalid/missing amino acid numbering SEQID (1) POS (141)
E	323	Invalid/missing amino acid numbering SEQID (1)at Protein (145)
E	323	Invalid/missing amino acid numbering SEQID (1) POS (146)
E	323	Invalid/missing amino acid numbering SEQID (1) at Protein (150)
E	323	Invalid/missing amino acid numbering SEQID (1) POS (151)
E	323	Invalid/missing amino acid numbering SEQID (1) at Protein (155)
E	323	Invalid/missing amino acid numbering SEQID (1) POS (156)
E	323	Invalid/missing amino acid numbering SEQID (1) at Protein (160)
E	323	Invalid/missing amino acid numbering SEQID (1) POS (161)
E	323	Invalid/missing amino acid numbering SEQID (1) at Protein (165)
E	323	Invalid/missing amino acid numbering SEQID (1) POS (166)
E	323	Invalid/missing amino acid numbering SEQID (1) at Protein (170)
E	323	Invalid/missing amino acid numbering SEQID (1) POS (171)
E	323	Invalid/missing amino acid numbering SEQID (1) at Protein (175)
E	323	Invalid/missing amino acid numbering SEQID (1) POS (176)
E	323	Invalid/missing amino acid numbering SEQID (1)at Protein (180) This error has occured more than 20 times, will not be displayed
E	254	The total number of bases conflicts with running total, Input: 33271, Calculated: 33171 SEQID(1)
E	342	'n' position not defined found at POS: 35360 SEQID(1)

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Total Warnings: 277
Total Errors: 414
No. of SeqIDs Defined: 259

Error code	Error Description
E 342	'n' position not defined found at POS: 35361 SEQID(1)
W 333	tabs used in amino acid numbering SEQID (1)
E 330	Invalid protein , found in SEQID(1) POS (358) Invalid Protein: Gys
W 333	tabs used in amino acid numbering SEQID (1)
Е 254	The total number of bases conflicts with running total, Input: 37984, Calculated: 37983 SEQID(1)
Е 254	The total number of bases conflicts with running total, Input: 38044, Calculated: 38043 SEQID(1)
Е 254	The total number of bases conflicts with running total, Input: 38104, Calculated: 38103 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38164, Calculated: 38163 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38224, Calculated: 38223 SEQID(1)
Е 254	The total number of bases conflicts with running total, Input: 38284, Calculated: 38283 SEQID(1)
Е 254	The total number of bases conflicts with running total, Input: 38344, Calculated: 38343 SEQID(1)
Е 254	The total number of bases conflicts with running total, Input: 38399, Calculated: 38398 SEQID(1)
Е 254	The total number of bases conflicts with running total, Input: 38447, Calculated: 38446 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38495, Calculated: 38494 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38543, Calculated: 38542 SEQID(1)
E 254	The total number of bases conflicts with running total, Input: 38594, Calculated: 38593 SEQID(1)
E 254	The total number of bases conflicts with running total, Input:

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Total Warnings: 277

Total Errors: 414

No. of SeqIDs Defined: 259

Actual SeqID Count: 259

Error code Frror Description

Err	or code	Error Description
		This error has occured more than 20 times, will not be displayed
W	333	tabs used in amino acid numbering SEQID (1)
W	333	tabs used in amino acid numbering SEQID (1)
W	333	tabs used in amino acid numbering SEQID (1)
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W	333	tabs used in amino acid numbering SEQID (1)
W	333	tabs used in amino acid numbering SEQID (1)
W	333	tabs used in amino acid numbering SEQID (1)
W	402	Undefined organism found in <213> in SEQ ID (2)
W	402	Undefined organism found in <213> in SEQ ID (3)
W	402	Undefined organism found in <213> in SEQ ID (4)
W	402	Undefined organism found in <213> in SEQ ID (5)
W	402	Undefined organism found in <213> in SEQ ID (6)
W	402	Undefined organism found in <213> in SEQ ID (7)
W	402	Undefined organism found in <213> in SEQ ID (8)
W	402	Undefined organism found in <213> in SEQ ID (9)
W	402	Undefined organism found in <213> in SEQ ID (10)
W	402	Undefined organism found in <213> in SEQ ID (11)
W	402	Undefined organism found in <213> in SEQ ID (12)
W	402	Undefined organism found in <213> in SEQ ID (13)
W	402	Undefined organism found in <213> in SEQ ID (14)
W	402	Undefined organism found in <213> in SEQ ID (15)

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Elapsed: 0 hr(s) 0 min(s) 17 sec(s) 974 ms

Total Warnings: 277 Total Errors: 414 No. of SeqIDs Defined: 259

Error code	Error Description
W 402	Undefined organism found in <213> in SEQ ID (16)
W 402	Undefined organism found in <213> in SEQ ID (17)
W 402	Undefined organism found in <213> in SEQ ID (18)
W 402	Undefined organism found in <213> in SEQ ID (19)
W 402	Undefined organism found in <213> in SEQ ID (20)
W 402	Undefined organism found in <213> in SEQ ID (21) This error has occured more than 20 times, will not be displayed
E 253	The number of bases differs from <211> Input: 20 Calculated:19
E 253	The number of bases differs from <211> Input: 25 Calculated:24

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      Alonso Karlezi, Alberto
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       Castillo Fernandez, Sergio
       Martinez Martinez, Antonio
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<140> 10542937
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<223> n at position 35360 represents aau, aac or aat
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<223> n at position 35361 represents aau, aac or aat
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